REMARKS

Claims 32 and 102-126 are pending in this application. Claims 105, 109, and 113-125 have been withdrawn by the Examiner as being drawn to non-elected species.

Claims 32, 102-104, 106-108, 110-112 and 126 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Rosenblum et al. (U.S. Pat. No. 5,846,966), The Medical Letter on Drugs and Therapeutics, 1998, Vol. 40, Issue 1030, pp. 68-69 (hereinafter "Medical Letter"), and Ambrosioni et al. (European Journal of Epidemiology, 1992, Supp. 1, pp. 129-133). For brevity, reference is made to the reasons for rejection set forth at pages 2-4 of the Office Action. This rejection is respectfully traversed.

The present invention is directed to a triple combination treatment composition of a sterol absorption inhibitor (such as ezetimibe), a PPAR activator (such as fenofibrate), and at least one cardiovascular agent (such as an ACE-inhibitor like captopril).

Rosenblum discloses that certain sterol absorbtion inhibitors, like ezetimibe, lower serum cholesterol levels and inhibit the intestinal absorption of cholesterol so as to significantly reduce the formation of liver cholesteryl esters and the risk of atherosclerosis. (Rosenblum, col. 20, lines 39-40).

Medical Letter teaches fenofibrate as useful in reducing VLDL cholesterol and triglycerides (Medical Letter, page 68). This reduction in triglycerides shifts the sub-group of LDL cholesterol to one that is less atherogenic. *Id.*

Ambrosioni is directed to ACE-inhibitors, and more specifically captopril and cilazapril, and their effect on atherosclerosis pathogenesis. While Ambrosioni indicates that the mechanism by which ACE-inhibitors act on atherosclerosis pathogenesis remains unclear, it does note that any anti-atherosclerosis effects provided by captopril are not due to the lowering of serum cholesterol levels. (Ambrosioni, page 130). In fact, Ambrosioni references a study in which the serum cholesterol levels in captopril-treated rabbits was actually higher than the serum cholesterol levels of untreated rabbits. *Id.*

In the Office Action, it is alleged that one skilled in the art would find it obvious to incorporate ezetimibe, fenofibrate, and captopril together in a single composition because the cited art teaches that each of these compounds are, individually, useful in reducing cholesterol and lowering the risk of atherosclerosis. In support of this proposition, the Office Action cites the case of *In re Kerkhoven*, 205 U.S.P.Q. 1069 (CCPA, 1980). However, the facts of this case are distinguishable from *Kerkhoven*. In *Kerkhoven*, each of the combined compounds was previously known to be separately used for the same purpose. *Id.* at 1072. Consequently, the court held, combining them to form another compound used for the very same purpose flowed logically from their use in the prior art. *Id.* Here, however, Applicants' inventive combination simply would not logically flow from the discussion of the individual compounds in the cited art. Most notably, as previously mentioned, Ambrosioni teaches that captopril actually causes an *increase* in the serum cholesterol level of a subject. Meanwhile, Rosenblum teaches that ezetimibe has the completely opposite effect, namely *lowering* serum cholesterol levels. One of ordinary skill in the art would not have found obvious the combination of a serum cholesterol lowering agent, like ezetimibe, with another agent, such as capitopril, that is known to raise serum cholesterol levels. *See, e.g., Ex Parte Bokisa*, 1997 WL 1897871, *3 (Bd. Pat.App. & Interf., 1997) (combination of known compounds not obvious when prior art indicates that one compound exhibits undesirable effects while the other compound minimizes these effects). This is especially true in light of Rosenblum's teaching that lowering serum cholesterol levels is likely to inhibit the progression of atherosclerotic lesion formation. (Rosenblum, col. 1, lines 37-41).

Absent a rationale explaining why, despite the contrary teachings in the cited art, one of ordinary skill would find it obvious to combine the three recited compounds into a single composition, a rejection under 35 U.S.C. § 103(a) simply cannot stand. Consequently, Applicants respectfully request the reconsideration and withdrawal of the pending rejection.

CONCLUSION

For all of the foregoing reasons, Applicants submit that pending claims 32 and 102-126 are patentable over the cited references and are in condition for allowance. Accordingly, reconsideration of the rejections and allowance of pending claims 32 and 102-126 are respectfully requested.

Should the Examiner have any questions regarding any of the foregoing or wish to discuss this application in further detail to advance prosecution, the Examiner is invited to contact Applicants' undersigned representative at the telephone number provided below.

Respectfully submitted,

By _____

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